

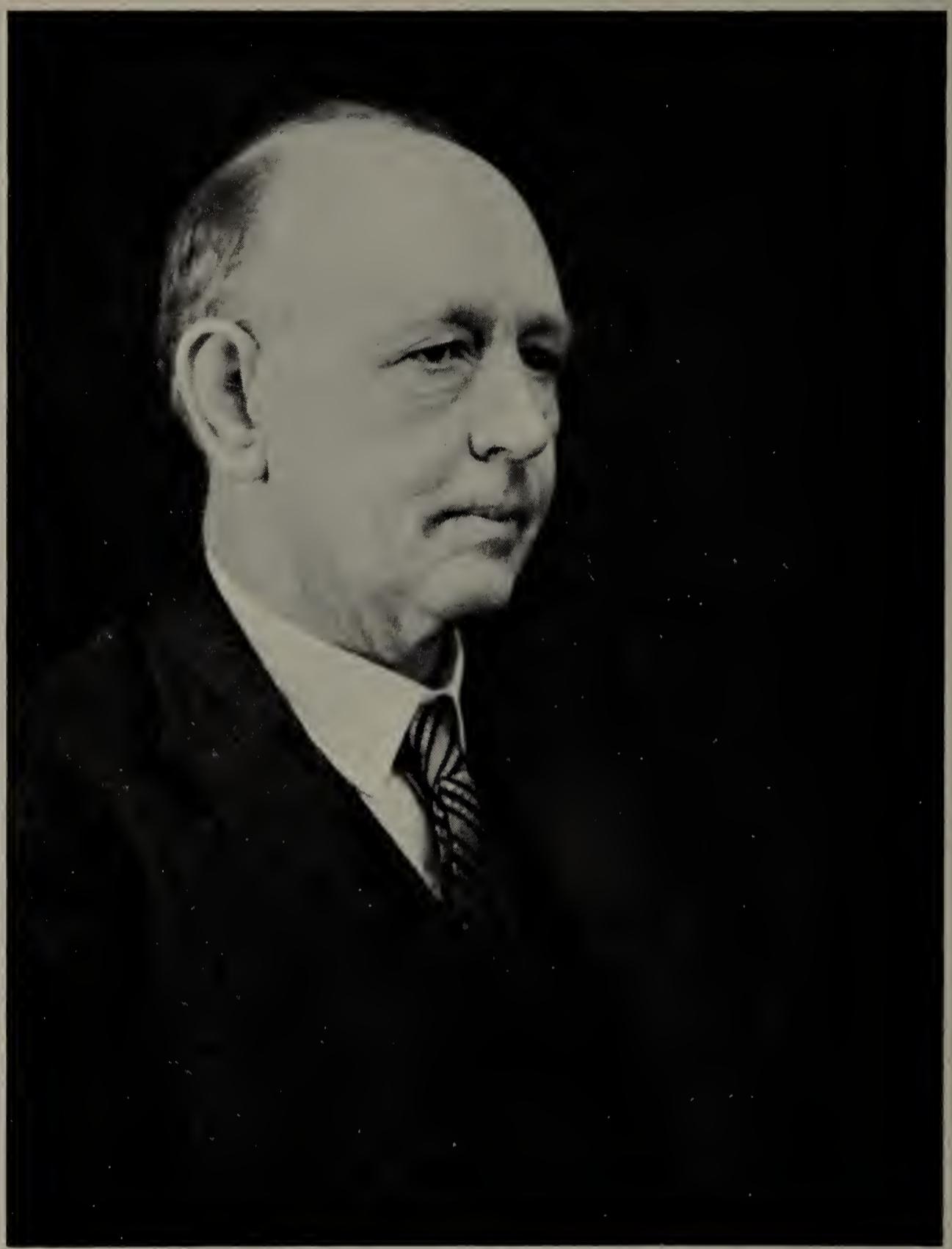
# CHARLES HALLILEY KELLAWAY

1889-1952

[Reprinted without change of pagination from  
*Obituary Notices of Fellows of The Royal Society*,  
Volume 8, November 1953]







Charles H. Kellaway

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### *Parentage*

CHARLES KELLAWAY was born on 16 January 1889, in the parsonage attached to the pro-Cathedral of St James, Melbourne (Victoria), where his father was then curate to the Dean, Hussey Burgh Macartney. The father, Alfred Charles Kellaway, had been born at Swanage, Dorset, in 1856, of parents who came from Lulworth; but on his seventh birthday, 23 September 1863, his mother had embarked with him for Australia, whither his father had apparently preceded them, to start anew as a farmer in Victoria. The venture cannot have prospered greatly, since Alfred Kellaway, the father of Charles, became a teacher in the State Education Department and thus supported himself through his University course, graduating with honours in history and political economy, before he was ordained and entered upon his main career in the Church. After holding the curacy above mentioned he became Vicar of All Saints Church, Northcote—a parish in the Melbourne suburbs. His wife, Anne Carrick Roberts, Charles Kellaway's mother, had been born at Longford, Tasmania, in 1854. Her parents had emigrated first to New Zealand, from there to Tasmania, where her father's elder brother was a well-known solicitor in Hobart, and finally, in 1870, to Melbourne. Her father, Richard Roberts, was the younger son of a Welsh anglican clergyman, and had married Frances Halliley, from whom Charles inherited not only his second name, but also his only ancestral link with the natural sciences; for she was the daughter of a north-country manufacturer who had had an interest in chemistry, and had been a friend of John Dalton.

### *Schooling and University in Melbourne*

Charles Kellaway was the eldest son and second child in a family of five—three sons and two daughters. He spoke in after years with affectionate gratitude of the puritan atmosphere of his upbringing in the parsonage, and of the self-sacrifice accepted by his parents for the education of their family—secondary schooling for all five, followed by a university course for four of them; an heroic achievement, indeed, even in those days, on a clerical stipend of never much more than £300 a year! Charles and his elder sister were taught at home by their father up to the age of 11, while

their mother's sister, whom he described as 'a cultured and delightful maiden aunt', cared for the primary teaching of the other three. Then Charles went to the Caulfield Grammar School for a year, and from there with a scholarship to the Melbourne Church of England Grammar School till he was 17 (1906). The latter school must have included a more adequate provision for the natural sciences than many grammar schools of those days; for we find him passing the Senior Public Examination in Physics and Chemistry with 1st Class Honours in his last year there. In the same year he won the Clarke Scholarship, which should have taken him to Trinity College, Melbourne University; and anybody who knew Kellaway in later years will feel sure that his eagerness for all kinds of healthy activity, physical and intellectual, would have enabled him to give and to gain more than most young men from such an experience of corporate college life. The strain on the family budget, however, made it impossible for him to accept it, and he went through his university course as a home-boarding student. It cannot be doubted that he took, nevertheless, the fullest part allowed by these conditions, in all the aspects of university life; but, in addition to the aid received from money prizes which he won, he had to eke out his slender resources by coaching juniors, and, even so, to complete his course with borrowed money. He had passed his preliminary scientific examination, with 1st Class Honours and a prize in organic chemistry, by 1907; and from then onwards his record shows him at the head of the year's list at each stage of the medical curriculum. He graduated M.B., B.S., in 1911, at the age of 22, winning the Jamison Prize in clinical medicine and a scholarship in obstetrics and gynaecology. The university teachers of whose influence on his achievement, then and later, he retained a special memory, were Sir David Orme Masson, F.R.S. (chemistry), Professor W. A. Osborne (physiology), and Sir Henry Carr Maudsley, K.C.M.G. (clinical medicine). From 1911-13 he held the usual appointments as Resident Medical Officer and Registrar at the (now Royal) Melbourne Hospital. In 1914 he became Tutor in Physiology at Trinity College, Melbourne, and, in the earlier months of 1915, acting Professor of Anatomy in the University of Adelaide, as deputy for a professor absent already on war duty.

*Service with A.A.M.C., 1915-1918*

Before the end of 1915, however, Kellaway himself left Australia, as a Captain, A.A.M.C., for service with the Australian Expeditionary Force, first in Gallipoli and then, in 1916, in the laboratory attached to the Third Australian General Hospital, in Cairo. Here he came for the first time under the stimulating influence of C. J. Martin, F.R.S., and received from him his first training in the research methods appropriate to the laboratory's special services to the hospital and the armies, in the fields of pathology and bacteriology. Dr (now Sir Charles) Martin, then Director of the Lister Institute in London, was serving, with the rank of Lt.-Colonel, R.A.M.C.,

as Pathological Adviser to the Armies in the Mediterranean Area, and therewith renewing old contacts with many friends and former pupils from Australia.

Kellaway went, in due course, with the Australian Forces to the Western Front, and there, in 1917, while he was serving as a Regimental M.O. with the 13th Australian Infantry Battalion, his gallantry in action won for him the award of a Military Cross. In the same year he lost his younger brother, Francis Gerald, who had abandoned his university course to enlist in 1914, had served in Gallipoli and France, had been given a commission and also awarded a Military Cross, and was then killed at Zonnebeck in 1917. Charles himself emerged by no means unhurt from the war; he took such a dose of phosgene in a gas-attack that, after a time in hospital, he was judged to be unfit for further active service; and, indeed, he was left, thus early in life, with a liability to bronchitis, which never altogether left him, though his energy and his eager enjoyment of life were still above the common level.

### *First visit to England*

When he was fit to travel, Kellaway, now a Major, was sent early in 1918 to London, to act as a Specialist Officer on Medical Boards for the Australian Flying Corps. These duties occupied only a small part of his time, and he was instructed to find opportunity also for research on the then new physiological problems of high flying, and, in particular, on the general effects of the sudden spell of low oxygen tension and resulting anoxaemia, to which the airmen of those early days were liable to be exposed. He came to see me, with Martin's recommendation, in the suite of laboratories in the Lister Institute, then housing my department of the projected National Institute for Medical Research, which had come into existence only a month before the outbreak of the war and before its more permanent accommodation was ready. There could be no thought of obtaining, in 1918, after nearly four years of war stringency, any of the elaborate equipment with which the general problem, then presented to Kellaway, has since been so thoroughly and directly investigated on the human subject. I was easily captured, however, by his modesty, his eagerness, his readiness to make a beginning on one aspect of a large problem, and his competence in improvising the means for such a limited experimental approach, with the small resources which I could make available. He decided to take the rises of the blood-sugar level, consequent upon the breathing of air-nitrogen mixtures with graded low proportions of oxygen, as a measure of the disturbance of the general balance of physiological functions by anoxaemia. Having standardized his method for producing anoxaemia thus in the cat, Kellaway proceeded to investigate the respective parts played, in producing the hyperglycaemic sequel, by the effect of the anoxaemia on brain centres giving rise to splanchnic nerve impulses; by its direct effect on the adrenal medulla, still causing some output of adrenaline even after division of the

splanchnic nerves; and, finally, by its direct effect on the liver cells, after section of the splanchnic nerves and extirpation of the adrenal medulla as well. It was no simple or easy undertaking for a man embarking upon his first independent attempt at experimental research. It involved skill, resourcefulness, and a large number of accurate determinations; but Kellaway's keenness, aptitude and conscientious industry were equal to its demands. The results were published in 1919 (4)\*, in a paper which established him, I think, as an experimental physiologist of potential distinction.

This first period of my association with Charles Kellaway, though it did not last long, laid for me the foundation of a friendship which lasted and grew with the passage of time. He seemed younger than his years, with his keenness and his breezy humour, and his tags of a vivid, if not always genteel, Australian slang. We were all becoming conscious then of a blessed relief from the long strain, as the tide of the war began to turn. When he and I managed to steal a few days of holiday together, I took him down to Chiddingfold in Surrey, where my wife and children were staying, and he was at once in high favour with all in our small family circle. The visit gave him also his first impression of the English countryside at close quarters, and the memory of it stayed with him.

#### *Australia, 1919-20*

As soon as demobilization and transport facilities made it possible, Kellaway was on his way back to Australia, early in 1919; and on arrival there he became, for a time, Acting Professor of Physiology at Adelaide. In 1920, however, the Royal Society's Foulerton Research Studentship fell vacant. Kellaway was appointed, and asked to be allowed to begin his tenure of the Studentship in my department of the National Institute, then recently reconstituted in its own building at Hampstead. I welcomed his application, and he was soon on his way to England again. Some months earlier he had married Miss Eileen Ethel Scantlebury, the youngest daughter of a medical practitioner in the Melbourne neighbourhood, so that we were able to welcome his wife with him at Hampstead, and he was still working with me there when their eldest son was born.

#### *Return to England as Foulerton Research Student, R.S., 1920-23*

Kellaway's first work as Foulerton Student dealt with a rather curious observation, made by McCarrison, that the adrenal glands of a pigeon fed on polished rice are not only enlarged in size and weight, but contain more than the normal load of adrenaline. He was able to confirm the main facts, and to show that the increase of adrenaline was due to the deficiency of vitamin B in particular, and not to that of protein, fat, or vitamin A. He interpreted the result as due to the lowering of general metabolism, and the

\* The figures in brackets in the text refer to the bibliography at the end.

consequently diminished call on the glands for output of the adrenaline which they formed (5). It was a careful piece of work, but dealt with a limited theme, giving him no lead into a wider field and no promise of a continuing interest.

As soon as he had finished this minor research, Kellaway began a more extensive one in close collaboration with me. This dealt with anaphylaxis in the guinea-pig, on which I had published my own first experiments some two years before the war. Together we made a further and more critical study of the response to the specific antigen of the isolated plain muscle of the uterus from anaphylactic guinea-pigs; and we confirmed my earlier conclusion, which Richard Weil had reached independently by experiments on the living guinea-pig, attributing the anaphylactic condition in this species to the predominant fixation to the plain muscle fibres of a specific, precipitating antibody. The same antibody, when present in excess in the body fluids, or in the saline medium in which, in our experiments, the isolated organ was suspended, completely protected the plain muscle from the antigen to which it had been sensitized, and thus produced a condition of true immunity. It seemed to Kellaway and me that our experiments demonstrated, beyond question, this relation of anaphylaxis to immunity in the guinea-pig, as dependent upon a difference of distribution of the same antibody between the fixed tissues and the body fluids. We felt it to be our duty, nevertheless, to make further enquiry into the nature and the modes of action of the various so-called 'anaphylatoxins'—products of incubating blood serum from normal guinea-pigs with various colloids and suspensions. Such preparations were at that time the subject of a formidable literature in support of an alternative conception, which represented the anaphylactic reaction in the guinea-pig as due to the liberation of a poisonous product of protein cleavage in the circulating blood. Kellaway and I found that we had embarked upon a laborious and intricate investigation; but the results only confirmed our confidence in the conclusions which we had drawn from our own positive experiments. For we found no evidence of a protein cleavage in those 'anaphylatoxins' which, on intravenous injection into normal guinea-pigs, produced reactions with a deceptive, though still only superficial, similarity to those seen in the true anaphylactic reaction; nor did these preparations, on direct application to the isolated plain muscle, produce such responses of tonus as they should have evoked, if they had contained the supposed direct agent of the anaphylactic shock. I think that this work, which Kellaway carried out with me, did something to divert research on anaphylaxis from what threatened, at that time, to be a misleading objective. We presented all these results together to the Royal Society, in a single paper of such length that it had to be published in the *Philosophical Transactions* (7). I think that we should have been wiser to cut it into several papers, of dimensions suitable for the *Proceedings*, to which its matter was more appropriate.

When Kellaway left me he went, still holding his Foulerton Studentship,

to Sir Charles Sherrington's Department of Physiology at Oxford, where he also did part-time duty as a Demonstrator. His stay there was but a short one, however, and the only record of research which he published from it described a failure to confirm a current suggestion, that the blood of frogs deprived of the adrenal glands had a muscarine-like action. Some work of my own on the esters of choline had led him to look for a substance of that type; but he found no activity of any kind (8).

From Oxford Kellaway returned to London, still holding the Foulerton Studentship, to work in the Medical School of University College Hospital under T. R. Elliott, F.R.S., then Professor in the Unit of Clinical Medicine there. His first and principal immediate collaborator was S. J. Cowell, then an Assistant in the Unit, and the first subject of their joint investigation was the antagonism to the shock-like effects of histamine exercised by some function of the adrenal glands (9, 10). I had myself drawn attention to the antagonism some years earlier, but had left undetermined the respective parts played in it by the medullary secretion of adrenaline and by the then unknown activities of the cortex. Kellaway and Cowell confirmed my own guess that the cortex had the main responsibility for the maintenance of a general resistance to histamine, and to tissue injuries—a conclusion not without some bearing on much more recent developments; but they also demonstrated the accelerated output of adrenaline in response to injections of histamine, and the importance of adrenaline in checking the concentration of the blood by loss of plasma, which even small doses of histamine were found to produce in its absence. For this they developed a technique of selectively destroying the medulla, by implanting tubes of radon. The same workers next turned their attention to anaphylaxis in the guinea-pig, dealing with certain problems left over from Kellaway's earlier work with me; and they recorded the results of their very thorough investigations of these in two papers, which added substantially to knowledge of the phenomena in question (11, 12). Still in the University College Medical School, Kellaway collaborated with T. A. Hughes in an early observation of the action of insulin, then still a novelty, on the metabolism of a normal human volunteer (13), and with the late A. E. Boycott, F.R.S., the Professor of Pathology, in experiments, negative in their results, on an alleged compensatory hypertrophy of the remaining suprarenal gland in the rabbit, when one had been removed (14). He had certainly made a full use of the opportunity offered by the Foulerton Studentship, for extending the range of his experience over a variety of subjects, mostly on the borderland of physiology, biochemistry and pathology; and the appointment as First Assistant in the Medical Unit, which he then accepted from Professor Elliott, would have extended it further in a clinical direction. Not long afterwards, however, came another opportunity, and the most important one in Kellaway's scientific career, when a vacancy occurred in the Directorship of the Walter & Eliza Hall Institute for Research in Pathology. This was a relatively new foundation in his native Melbourne; the retiring Director, Dr S. W. Patterson, who was

accepting a clinical appointment in Wales, having been in office for only four years. Kellaway's qualifications for such a post had now become clear, and, being duly appointed, he held the post for the next 21 years. During that period he had the satisfaction of seeing the Institute, under his stimulating and generous leadership, become the leading Australian centre, and one of high rank among those in all the world, for researches in Experimental Pathology and in the related fields of medical science.

*Director of the Hall Institute, Melbourne, 1923-1944*

Towards the end of 1923, therefore, Kellaway returned to Australia, with the good wishes of a now wide circle of friends in England, to take up his new appointment and enter upon the main phase of his life's work. His duties as Director would certainly have brought him, in any case, a substantial burden of administrative duties. The Institute's research activities, however, were growing in volume and scope, under Kellaway's stimulating leadership, during the whole period of his Directorship; and, as in all such cases, the call for additional accommodation and equipment was continuous, while the financial needs showed a more than proportionately rapid expansion. The Director of such a developing organism must have found himself involved in much work of adjustment and contrivance, while the urgent quest for further endowments, to ensure that the Founders' generosity should be continuously effective, must have made large additional demands upon his energy and his powers of convincing advocacy. Support was forthcoming, indeed, from the Commonwealth Government, the Rockefeller Foundation and the National Health and Medical Research Council of Australia, as well as from a number of private donors who had come to know Kellaway and to trust him. His personal modesty, frankness and integrity counted for much in the success of such appeals and negotiations. As has been well said by friends who were close to him at the time, 'The Institute was accepted by the people of Melbourne first as a local and later as a national asset; by scientific workers it came to be regarded as the keystone of medical research in Australia.' In this successful work as Director of the Hall Institute, Kellaway certainly rendered one of the greatest of his services to medical science; and his final task, before he came again to England in 1944, was its transfer to new buildings at Parkville, forming a wing of the Royal Melbourne Hospital. By this transfer the Institute came into a closer relationship, not only with the Hospital, but with Melbourne University. And there Kellaway was able to hand over its control, with full confidence, to his distinguished successor, Sir F. Macfarlane Burnet, F.R.S., who had himself served his apprenticeship and achieved his world position in medical research as a member of the staff of the Institute under Kellaway's Directorship.

At a fairly early stage, Kellaway's services began to be sought also for official advice to the Federal Government, and later to the Australian Army. Yet, through it all, except when the outbreak of the Second World War

required him again for service with the Australian Army, he always had research in hand, with a succession of collaborators, and the results appeared in an impressive series of publications, as can be seen in the bibliography at the end of this article. In 1927 he published (32) in the *Medical Journal of Australia*, an account of the growth and activities of the Hall Institute since its war-time foundation in 1916, with Sir Harry Allen as its Honorary Director for the first three years, with Patterson as its first full Director till 1923, and then with Kellaway himself for the further 4 years to the date at which he wrote his review. The original benefaction had evidently been intended mainly to make better provision for the pathological and bacteriological examinations required by the regular clinical work of Melbourne (later the Royal Melbourne) Hospital, and for such researches, no doubt, as might arise from opportunities presented in the course of this routine. Already by 1927, however, the Institute, under Kellaway, had acquired a relative independence and a greatly extended scope for its enterprise in research. The regular diagnostic and analytical work for the hospital was now accommodated mainly on the ground floor of the building, which provided research laboratories for physiology and biochemistry on its first floor, a library and research laboratories for bacteriology and immunology on its second floor, and workshops and optical dark-rooms in its basement. By the time that Kellaway published his review, the list of his other publications shows that, with various collaborators, he had already laid down the principal lines of his co-operative researches for some years ahead. The functions and infections of the kidneys, and the origin of the proteins found in the urine in diseases of those organs, provided subjects for several papers published in that period (15, 18, 19, 23, 24, 25, 26). Another series (16, 17, 20, 22, 28, 29, 30, 31, 33), dealt with helminthic infections, and especially with hydatid disease, which occurs with such relative frequency in the sheep-farming community of Australia. In the work of both these series Kellaway was able to make use of the experience of immunology, and especially of the experimental technique of anaphylaxis, which he had acquired during his stay in London; and as late as 1932, with K. D. Fairley (59), we find him returning to a survey of the clinical significance of the laboratory tests then available for hydatid disease.

#### *Australian snake venoms*

Meanwhile, however, he had begun, in 1929, the series of researches, with a number of different partners, on the venoms of the Australian colubrine snakes, and of certain other species. These studies of the detailed actions of venoms occupied a central position in his research interests for the next eleven years or so, until the demands of the second world war gave a different turn to his activities. A reference to the bibliography at the end of this notice will show the extent to which researches on the venoms and their actions predominated in Kellaway's scientific publications between 1929 and 1940. C. J. Martin had earlier made fundamental studies on the

actions of the venoms of some of the principal Australian colubrine snakes, and especially on their actions on the blood, including those due to the presence in them of extremely potent fibrin ferments, leading to intravascular clotting, or, with smaller doses, to loss of the power of the shed blood to clot. Kellaway and his team threw their net as widely as possible, examining the actions of as many snake venoms as they could obtain and, in addition, of the venoms of certain spiders, of bees and of the poison-claw of the monotreme platypus (*Ornithorhynchus*). The details of this work on the varying symptomatology of the effects produced by these different poisons, in different victim species, can only be studied in the original publications. All the venoms of the Australian colubrine snakes examined were found to contain, in different proportions, a thrombase, a haemolysin, a haemorrhagin and a neurotoxin, of which the latter was the cause of death when the venoms were injected hypodermically. A valuable survey of some of the results of these widely ranging investigations was given by Kellaway in his Dohme Lectures in Baltimore, in 1937 (93). Particular mention may here be made of two other directions in which they appear to have broken new ground, in dealing with aspects of the action of these naturally poisonous proteins which had not hitherto received so much attention. One was a direct peripheral action producing, among other effects, a reversible curare-like paralysis of voluntary muscles in frogs and mammals (62, 63, 64, 70). A lead to the study of another feature of the actions of all these poisons may be traced to Kellaway's earlier participation in experiments on the mechanism of anaphylaxis. By 1929, when his study of the venoms began, evidence had converged from various sources to show that the symptoms of the anaphylactic reaction are not due only to the directly injurious action of the re-injected antigen, on the cells which have acquired the specific sensitiveness to it, but also, and often in large measure, to the secondary actions produced on cells of other types by intensely active substances released from those primarily injured. Among the normal constituents of active cells which, on such release, would be expected to make a conspicuous and characteristic contribution to the syndrome of the anaphylactic reactions, as seen in the different species, was histamine; and among several groups of workers who, in the following years, had indeed succeeded in obtaining direct evidence of such a release of histamine in the anaphylactic reactions of different types, was one which, in 1932, was led by W. Feldberg in Berlin. Later again, after some years in my own laboratory, Feldberg had accepted from Kellaway a research appointment in the Hall Institute. In 1937-38, therefore, they were able to collaborate in a series of experiments, designed to determine whether the snake venoms and related animal poisons would also liberate histamine and other significantly active normal constituents from the cells of the different organs which they directly poisoned, and how far the actions of the substances thus liberated would contribute to the complex of resulting symptoms. The actions of histamine having been recognized as making a major contribution to the anaphylactic reaction, it was natural first to

enquire whether this substance was also released by the more generalized and drastic action of the venoms on the body cells. The affirmative answer to this question is to be found in a series of papers, dealing largely with experiments on perfused organs, by Feldberg and Kellaway (86, 88, 89, 90, 91, 92, 94, 95), in which the parts played by the action of this liberated histamine, in the actions of the venoms on normal animals of different species, are also fully discussed. The factors were not, in any case, easy to disentangle completely; for, not only were the effects of the liberated histamine complicated by a slower, direct action of the venom itself on the test preparation (guinea-pig jejunum); it was necessary also, especially in studying the action of cobra venom, to take account of the effect of 'lysocithin'—a haemolytic derivative of the widely occurring lecithin, long known to be produced by the action upon the latter of a lecithinase which the cobra venom contains. The demonstration of such a secondary component, in the physiological effects of the one venom in which such an enzyme action had been recognized and fully studied, might have raised the question of its occurrence in the actions of other venoms, such as those of the Australian snakes with which the investigation began. The authors, however, might well shrink from embarking on such an indefinitely extensive programme of highly specialized research. They were, in fact, more concerned to emphasize the fact that, apart from the contributions to the general complex of symptoms made by the direct actions of the venom itself, or by those of such a product of its enzymatic action, there were substances other than histamine preformed in the normal living cells, released like it by the primary, injurious effect of the venom, and capable also of making a significant contribution to the full range of the resulting symptoms. Feldberg and Kellaway were interested, in particular, in the occurrence, in addition to histamine, in their perfusates from 'envenomed' organs, of a slowly-reacting stimulant of smooth muscle, of larger molecular dimensions and apparently of a peptide nature. There was no pretence at a chemical definition of this 'slow-reacting substance'; but the attention which they gave to it may be regarded, perhaps, as having given some impetus to more recent studies by a number of observers of such physiologically active constituents of normal cells, apparently released with histamine as the result of many types of cell injury, and making various, though often minor, contributions to the resulting syndrome.

Kellaway had been concerned, however, not merely with such a finer analysis of the effects of these venoms from snakes and other animals. Such studies had been incidental, in fact, to his plans for a more effective provision for the treatment of the very dangerous and not infrequently fatal bites of the Australian snakes (56, 98). He had studied the efficacy of local venesection as an item in such treatment (51, 52), and he had carried out researches on the specific antitoxins against some of the most dangerous Australian venoms (55). It was most fortunate, indeed, that he had such an antitoxin immediately available, when he himself was bitten by a fully venomous Australian tiger-snake (*Notechis scutatus*), which he was handling

with a view to obtaining a supply of its venom for experimental use and antitoxin production. A large intravenous injection of the appropriate antitoxin was given promptly, and may be credited with the saving of his life, though only at the cost of a secondary menace to it, in the form of a severe anaphylactic reaction. This included such a threatening oedema of the glottis that surgeons were standing by for some hours, ready to perform tracheotomy if it should be needed. Kellaway could, therefore, make an unusually good claim to first-hand, personal experience of two of the main subjects of his own researches—the action of Australian snake venoms and the acute anaphylactic reaction.

#### *Further researches and war service*

Mention has been made of Kellaway's advisory service to the Federal Government on a number of occasions. On one of these he acted, in 1928, as Chairman of a commission appointed to investigate a disaster at Bundaberg, in Queensland, in which a group of children who had received injections from a particular bottle of a diphtheria prophylactic, had died from a resulting septicaemia. The investigation which Kellaway conducted with his colleague and successor, F. M. Burnet, produced most valuable evidence of the conditions under which such a preparation, sterile at the time of issue, but not containing an efficient antiseptic, could become a culture-medium for organisms accidentally introduced at the withdrawal of an initial dose from a multiple container, and a consequent source of danger to those injected later in a series. An incidental outcome was the determination (45) of the conditions under which a staphylococcus can be made to produce a potent exotoxin in artificial culture, and thus to provide material for an efficient immunizing antigen and an antitoxin against this organism. The recognition of the cause of the Bundaberg tragedy is reflected in provisions of the Therapeutic Substances Act, now controlling the preparation of such remedies for issue in this country.

Before Feldberg returned to an appointment in England, in 1938, the evidence of the part played by the liberation of histamine in the actions of venoms had been extended to other poisons—staphylococcus toxin and even mercuric chloride (95). Thereafter Kellaway was engaged, with Trethewie and others, in a more general study of the release of histamine and other natural cell-constituents in response to various physical and chemical injuries (96, 99, 101 to 106). Already the second world war had begun, and we find them turning their attention to the study of tissue injury, and the resulting secondary release of active cell constituents, by the toxins of the organisms of gas-gangrene and wound-infection. By this time, however, Kellaway, who had served as a part-time Director of Hygiene to the Australian Army H.Q. during a period between the wars, had accepted appointment again as Director of Pathology to the Australian Army Medical Service, with the rank of Colonel. For the first two years of the war he could

discharge the advisory duties of this post on a part-time basis, making available his exceptional knowledge of Australian workers in medical research, and the laboratory facilities at their disposal, while he still directed the activities of his own Hall Institute and organized them for special war services. Investigations and facilities were there promptly made available for techniques of diagnosis, the concentration and drying of sera, blood-typing and blood transfusion, shock and haemorrhage, immunization against influenza and, later, when Japan had entered the war, on scrub-typhus and Asiatic schistosomiasis. By 1941 it was natural that such a programme should have made contacts at many points with the war-time researches and enterprises which were being organized in Britain, and also in the U.S.A., well in advance of active American participation in the war. In 1941, therefore, Kellaway undertook a tour of duty in the U.S.A., on the way to Britain, in order to establish a more direct and intimate liaison between war-time medical research activities in these countries with those in Australia. I was then still living in Mount Vernon House, at Hampstead, as Director of the adjoining National Institute for Medical Research; and my wife and I rejoiced to find that Kellaway could make his headquarters there with us, when he eventually arrived in England. And so it came about that he was sitting with us on the evening of 7 December 1941 when the B.B.C. gave out the news of the Japanese attack on Pearl Harbour. For Kellaway the news came with a double shock of tragedy, in that it meant an indefinite interruption of all means of transport to Australia, while it created a new urgency for his presence there. Soon after he succeeded, early in 1942, in returning home, he relinquished his duties as Director of Pathology, to accept an appointment, with the rank of Brigadier, as scientific liaison officer on the staff of the Director General of the Australian Army Medical Service. This post he held for the next two years, and it brought him a full and exacting responsibility for a wide range of new and practical problems of pathology, physiology and medicine, entailed by the extension of the war into the tropics, and the rapid development in Australia of a principal base for the medical aspects of the operations of the Allied Powers in the Pacific area. The situation made an urgent call upon Kellaway, for all that he could give of imagination and enterprise in the promotion of researches, and of prompt efficiency in the application of their results.

*Director of the Wellcome Research Institution*

Two years later, in 1944, the urgency of this call for his services to Australia and to the whole Alliance was coming to an end, and Kellaway was free to accept an invitation to succeed the late Dr C. M. Wenyon, F.R.S., who was then retiring from the position of Director-in-Chief to the group of research laboratories maintained by the Wellcome Foundation Limited, with its headquarters in Euston Road, London. The change was made easier for him by the fact that his friend and colleague of many years, in peace and war,

Dr (now Sir) Neil Hamilton Fairley, F.R.S., was willing to accept appointment with him, becoming head of the Wellcome Laboratories for Research in Tropical Medicine, until he became the first incumbent of the Chair of Tropical Medicine, which the Wellcome Trustees had meanwhile endowed, at the London School of Hygiene and Tropical Medicine. So Kellaway came back to London once again, and, when the period of the V weapons had passed and the war at last reached its end, he was followed thither by his wife and three sons, two of them to continue their studies in Oxford and Cambridge respectively.

I feel sure that Kellaway had accepted the new appointment with an expectation that, after an inevitable period of readjustment, he would find it possible so to organize its administrative obligations as to leave him a fair margin of freedom for the resumption of the personal researches, which his war-time service had so largely interrupted. I myself had hoped that it might, indeed, be so. In the event, Kellaway found that the return of such a many-sided research enterprise, from highly specialized and urgently demanded war-time activities to a programme of normal range and freedom, called for a much heavier and continuous effort of reorganization than he had foreseen. He could not, indeed, have been expected to know in advance the scope and the variety of the responsibilities in which this period of readjustment would involve him, or the degree to which it would bring him into contact with analogous readjustments in the productive industry, which provided the means for the researches now under his direction. It soon became clear, in fact, that for some years ahead he would not be able to count on such a free remainder of time or thought, as might enable him to resume his own researches; and meanwhile he had promptly recognized, in the duties of his new position, a task worthy of all his energies, and of all his unusual gifts of character and personality, and he threw himself into it with a characteristic gusto. He was genial by nature, ready and generous with his understanding of the problems facing any of his colleagues, on the productive as well as the research side of the whole organization. He was unwearying in his effort to ensure the best conditions for the researches of those working under his direction, to strengthen their team by a wise recruitment, and to work with them in the construction of an enterprising and elastic programme of researches, helping them to hold the balance between fickle discouragement and obstinate persistence, or between too remotely academic an approach and too narrowly practical an aim. From the outset he won the confidence and the affection of all his associates and he seemed to adjust himself with remarkable ease and efficiency to conditions which must have been, in many directions, unfamiliar to him. Kellaway's competent grasp of all the activities of the research organization which he thus directed, his pride in its achievements and his enlightened vision of its further potentialities, will all be clear to any reader of the lecture which, a few years later, he gave by invitation to the Royal Society, on 'The Wellcome Research Institution' (115).

I do not think that we need to assume that medical science, on balance, suffered a serious loss through this diversion of Charles Kellaway's research activities, from the direct and personal contribution of his earlier years to the duties of advice and organization for the researches of others, which so completely absorbed his energies after 1944. Those workers in science, whose spring of original ideas still flows in full vigour after life's middle years, are probably exceptional in any case; and I am inclined to believe that Kellaway, at 55—the age at which he returned finally to London—had reached a stage at which he could do better service to the progress of science by the stimulus, the encouragement and the guidance, which his wide experience and his generous temperament so eminently qualified him to give to men of fresher minds and of more recent training in the newer disciplines, than any which he could have rendered by a predominant concern for researches of his own. Probably, like all of us, he continued to hope for the return of such a relative freedom as would have enabled him again to focus his own ideas on the devising, and again to use his own hands in the carrying out of an experimental attack on some problem; but even a partial return to such direct activity in research was most sadly to be denied to him. For, by the time that such a possibility might otherwise have been coming into view, a deterioration of his health had become all too obvious. He was long distressed and wearied by an intractable colitis, which seemed, however, inadequate by itself to account for the rapid change in his previously robust physique. His colleagues had eventually persuaded him to take a long spell of leave and had planned to send him to Australia, believing, on medical advice, that the complete rest in the familiar scene and the generous protein diet there available might set him on the road to recovery. All these arrangements were complete, when he was taken to hospital for an urgent operation, which in itself was not severe and was entirely successful in its object. Before he was discharged, however, a complete X-ray examination made as a routine revealed, almost by chance, an ominous shadow in his chest; and a further operation then showed this to be due to a tumour of the lung, already beyond the reach of removal.

Nothing in the whole of Charles Kellaway's career had been more worthy of the affectionate admiration with which so wide a circle of friends and colleagues had come to regard him, than the quiet courage with which he met this tragic discovery. He was determined to use to the fullest possible extent, for the discharge of the duties of his post, whatever span of life might still be his, so long as the inevitable decline of his physical vigour left him with any power of continued activity; and he calmly shaped his plans with this resolve in mind. As soon as the immediate effects of his operation had sufficiently subsided, he was back at his desk, eager again for contacts with all that was happening in his research organization, prompt and clear in his judgments, skilful even in evading the attempts of his colleagues to spare him. When he spoke to me on the telephone, the manner of his talk and the tone of his voice for long gave no hint of what he was facing; and if I visited

him, his buoyant spirits were readily at call, to hide, for a spell at least, the effects of his advancing illness. One of his first reactions to the news of his fate had been to express a hope that he might live to see another English spring, which he had loved since he first came here towards the end of the first world war. When the spring of 1952 came it was one of unusual beauty; and later he was able to enjoy more than one short revival of his waning strength from holidays spent in his favourite country sport of fishing. As his reserves of strength grew smaller, he slowly lightened his burden of duty and relinquished his active enjoyments; but he continued to rouse enough brief energy to let a visiting friend feel the familiar affectionate warmth of his greeting. So he went steadfastly and with unwavering courage to the end which he saw so clearly. He died on 13 December 1952.

Kellaway was elected F.R.C.P. in 1929, and a Foundation Fellow, R.A.C.P., in 1938. In 1932 he was awarded the Walter Parfitt Prize of the Royal Society of New South Wales. He was elected F.R.S. in 1940, and served on the Council from 1947 to 1949. From 1944 till his death he served as one of the Society's representatives on the Council of the Imperial Cancer Research Fund.

In writing this notice I have had the advantage of using the careful account which Charles Kellaway had himself furnished, in the Society's collection of personal records. Mrs Kellaway has been kind enough to read the manuscript, and my secretaries, Mrs Cutts and Miss E. Parker, have given me valuable help with the bibliography.

H. H. DALE

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